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Pesticide Fact Sheet Number 100
Azinphos-methyl (Guthion)

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This document contains up-to-date chemical information, including a summary of the Agency's regulatory position and rationale, on a specific pesticide or group of pesticides. A Fact Sheet is issued after one of the following actions has occurred.

1. Issuance or reissuance of a registration standard,
2. Issuance of each special review document,
3. Registration of a significantly changed use pattern,
4. Registration of a new chemical, or
5. An immediate need for information to resolve controversial issues relating to a specific chemical or use pattern.

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EPA

Pesticide Fact Sheet

Name of Chemical: Azinphos-methyl (Guthion)
Reason for Issuance: Issuance of Guidance Document
Date Issued: 9/30/86
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1. Description of Chemical

-Generic Name: O,O-dimethyl-s-[(4-oxo-1,2,3-benzotriazin-3(4H)-yl)methyl] phosphorodithioate
-Common Name: Azinphos-methyl
-Trade Names: metiltriazotion, carfene, cotion-methyl, gusathion, gusation-M, guthion, Bay 9027, Bay 17147, R-1582
-EPA Shaughnessy Number: 058001
-Chemical Abstracts Service (CAS) Number: 86-50-0
-Year of Initial Registration: 1956
-Pesticide Type: Insecticide, Acaricide, Molluscicide
-Chemical Family: Organophosphate
-U.S. and Foreign Producers: Bayer AG (Federal Republic of Germany), Makhteshim Chemical Co.(Israel), and Mobay Chemical Corporation (U.S.) and Aceto Chemical Company.

2. Use Patterns and Formulations

-Application sites: fruit and field crops, vegetables, tobacco, ornamentals and forest trees
-Types and methods of application: foliar (by ground or aerial equipment), ULV foliar application, soil application, transplant water application
-Application rates: 0.047 to 10.35 lb a.i./A
-Types of formulation: technical, formulation intermediate, dust, granular, wettable powder, emulsifiable concentrate, flowable concentrate, soluble concentrate
-Usual carriers: Confidential Business Information
-All liquid formulations with concentrations of 13.5% or greater are currently classified as restricted use chemicals

3. Science Findings

Chemical Characterisitics:

Technical azinphos-methyl is a yellow-brown solid with a melting point at around 63°C, that decomposes at elevated temperatures and is soluble in most organic solvents. The empirical formula is $C_{10}H_{12}N_3O_3PS_2$ and the molecular weight is 317.1.

Toxicology Characterisitics

-Acute oral: 4.4 mg/kg (rat), Toxicity Category I, highly toxic
-Acute dermal: 200 mg/kg (rat), Toxicity Category I, highly toxic
-Primary Eye Irritation: Data gap.
-Acute Inhalation: Data gap.
-Primary Skin Irritation: Data gap.
-Skin Sensitization: Data gap.
-Major Routes of Exposure: Handling of the concentrated pesticide and airblast application produce the largest exposure per pound of azinphos-methyl handled. Human exposure to azinphos-methyl from handling, application, and re-entry

operations would be minimized by the use of respirators and protective clothing.

-Oncogenicity: A mouse oncogenicity study showed that no increased incidence of tumors could be attributed to exposure to azinphos-methyl. A rat oncogenicity study, that was found to be uacceptable upon re-evaluation, showed that male rats developed tumors of the pancreatic islets and of the follicular cells of the thyroid. Because of the wide range of spontaneous incidence of these tumors in Osborne-Mendel rats, the Agency concludes that there is no clear link between the development of tumors to the administration of azinphos-methyl, the Agency is requiring that a rat oncogenicity study be conducted and submitted.
-Metabolism: Data gap.
-Teratology: Data gap.
-Reproduction: Data gap.
-Mutagenicity: Data gap.

Physiological and Biochemical Characteristics

-Mechanism of Pesticidal Action: Cholinesterase inhibition by all routes of exposure.
-Metabolism and persistence in plants and animals: Radiolabeled azinphos-methyl residues are absorbed through the roots and translocated to the shoot of hydroponically treated plants. Available data indicate that azinphos-methyl is relatively persistent on leaf surfaces and is gradually degraded to polar metabolites. Although the submitted studies are not adequate to assess the nature of azinphos-methyl in animals, metabolites of azinphos-methyl were identified in chicken excreta and rat urine.

Environmental Characteristics:

-Available data indicate that azinphos-methyl exhibits both low soil mobility and low leaching potential in a variety of soil types. Leaching studies indicate a low potential for leaching of azinphos-methyl residues to groundwater. In sandy soils azinphos-methyl dissipates in the field fairly rapidly and is metabolized by microorganisms.

The half-life of azinphos-methyl in a non-sterile soil is 21 days under aerobic conditions and 68 days under anaerobic conditions. It is more stable in sterile conditions with a half-life of 355 days. Under aerobic conditions the following azinphosmethyl metabolites were detected: oxygen analog residues, mercaptomethyl benzazimide, benzazimide, hydroxymethyl benzazimide, and bis-methyl benzazimide sulfide. Benzazimide and hydroxymethyl benzazimide, were identified as the major degradation products resulting from hydrolysis. Available photodegradation data are inadequate to assess the photodecomposition of azinphos-methyl.

-Re-entry: Treated areas may not be re-entered for at least 24 hours unless protective clothing is worn.

Ecological Characteristics

-Acute avian oral toxicity: Supplemental data indicate an LD_{50} of 136 mg/kg body weight for mallard ducks, 60-120 mg/kg for bobwhite quail, 74.9 mg/kg for pheasant, and 84.2 mg/kg for chukar. (Moderately toxic for all species tested).
-Avian dietary toxicity: LC_{50} = 488 ppm for bobwhite quail (highly toxic), LC_{50} = 639 ppm for Japanese quail (moderately toxic), and LC_{50} = 1940 ppm for mallard duck and 1821 ppm for ring-necked pheasant (slightly toxic).
-Freshwater fish acute toxicity (LC_{50}): Available data place azinphos-methyl in the range from very highly toxic to moderately toxic [LD_{50} values of 0.36-4,270 ug/l, depending on species tested with most values in the very highly toxic range (less than 100 ug/l)].
-Freshwater aquatic invertebrate toxicity: 0.13-56 ug/l, depending on the species tested (very highly toxic).

Tolerance Assessment

-Tolerances have been established for residues of azinphos-methyl in a variety of raw agricultural commodities in meat, fat and meat byproducts (refer to 40 CFR 180.154 and 40CFR 180.154a. for listing of tolerances), and in processed food (21 CFR 193.150) and and feed (21 CFR 561.180).
-The Agency is unable to complete a full tolerance assessment for the established tolerances due to residue chemistry and toxicology data gaps.
-No Mexican tolerances have been established for azinphos-methyl.

Commodity	U.S.	Canadian	Codex
Alfalfa	2.0	0.1	2.0
Alfalfa,hay	5.0	-	-
Almonds	0.3	-	0.2
Almonds,hulls	10.3	-	10.0
Apples	2.0	2.0	1.0
Apricots	2.0	2.0	2.0
Artichokes	2.0	0.5	0.5
Barley,grain	0.2	0.1	0.2
Barley,straw	2.0	0.1	-
Beans(dry)	0.3	2.0	0.5
Beans(snap)	2.0	2.0	0.5
Birdsfoot Trefoil	2.0	0.1	-
BirdsfootTrefoil,hay	5.0	0.1	-
Blackberries	2.0	2.0	1.0
Blueberries	5.0	2.0	1.0
Boysenberries	2.0	2.0	1.0
Broccoli	2.0	1.0	1.0
Brussels Sprouts	2.0	1.0	1.0
Cabbage	2.0	1.0	0.5

Commodity	U.S.	Canadian	Codex
Cattle,fat	0.1	-	-
Cattle,meat by product	0.1	-	-
Cattle,meat	0.1	-	-
Cauliflower	2.0	0.5	0.5
Celery	2.0	0.5	2.0
Cherries	2.0	1.0	1.0
Citrus fruits	2.0	2.0	2.0
Clover	2.0	0.1	-
Clover,hay	5.0	-	-
Cottonseed	0.5	-	0.2
Crabapples	2.0	-	1.0
Cranberries	2.0	-	-
Cucumbers	2.0	0.5	0.5
Eggplant	0.3	-	0.5
Filberts	0.3	-	-
Goats,fat	0.1	-	-
Goats,meat by product	0.1	-	-
Goats,meat	0.1	-	-
Gooseberries	5.0	-	-
Grapes	5.0	5.0	4.0
Grass,pasture	2.0	0.1	-
Grass,pasture,hay	5.0	-	-
Horses,fat	0.1	-	-
Horses,meat by products	0.1	-	-
Horses,meat	0.1	-	-
Kiwi fruit	10.0	0.4	4.0
Loganberries	2.0	2.0	1.0
Melons	2.0	-	2.0
Nectrines	2.0	-	1.0
Nut,Pistachio	0.3	-	-
Oats,grain	0.2	0.1	0.2
Oats,straw	2.0	-	-
~~Onions(green)~~	~~2.0~~	~~1.0~~	0.5
Parsley(leaves)	5.0	-	0.5
Parsley(roots)	2.0	-	0.5
Peaches	2.0	2.0	4.0
Pears	2.0	2.0	1.0
Peas,black-eyed	0.3	-	0.5
Pecans	0.3	-	-
Peppers	0.3	0.2	0.5
Plums	2.0	1.0	1.0
Potatoes	0.3	0.1	0.2
Quinces	2.0	2.0	1.0
Raspberries	2.0	2.0	1.0
Rye,grain	0.2	0.1	0.2
Rye,straw	2.0	0.1	-
Sheep,fat	0.1	-	-
Sheep,meat by product	0.1	-	-
Sheep,meat	0.1	-	-
Soybeans	0.2	0.2	-

Commodity	U.S.	Canadian	Codex
Spinach	2.0	2.0	0.5
Strawberries	2.0	1.0	1.0
Sugarcane	0.3	-	-
Tomatoes	2.0	1.0	0.5
Walnuts	0.3	0.1	-
Wheat,grain	0.2	0.1	0.2
Wheat,straw	2.0	0.1	-
Milk	0.04	-	-
Soybean oil	1.0	-	-
Dried citrus	5.0	-	-
Sugarcane bagasse	1.5	-	-

The data for azinphos-methyl residues in or on potatoes, parsley, pistachios, sugarcane bagasse and sugarcane are adequate to support the respective established tolerances.

Data are not adequate to support the established tolerance for residues in or on onions, celery, spinach, broccoli, Brussels sprouts, cabbage, cauliflower, beans, soybeans, peppers, tomatoes, cucumbers, melons, citrus fruit, apples, apricots, cherries, nectarines, peaches, plums, blackberries, blueberries, cranberries, grapes, strawberries, almonds, almond hulls, filberts, pecans, walnuts, wheat grain, wheat straw, pasture grass, alfalfa, clover, artichokes, cottonseed, kiwi fruit, eggplant, crabapples, pears, quices, boysenberries, loganberries, raspberries, oat grain, rye grain, barley grain, oat straw, rye straw, barley straw, birdsfoot trefoil, soybean oil, and dried citrus pulp.

A Provisional Limiting Dose (PLD) based on a 2 year dog feeding study has been established using a uncertainty factor of 100. The Maximum Permissible Intake (MPI) is 0.075 mg/kg for a 60 kg. person. The Theoretical Maximum Residue Contribution (TMRC) to the human diet from the existing tolerances is 0.6678 mg for a 1.5 kg diet which is 899% of the MPI. (This value is greatly inflated when compared to actual dietary residues expected in practice, and is due solely to the additional 10-fold uncertainty factor applied for the reduced data base and two-fold increase in sensitivity of the dog compared to that of the rat). When the required chronic feeding studies are submitted, the PLD and TMRC will be re-evaluated.

-Reported Pesticide Incidents: The Pesticide Incident Monitoring System (PIMS) reported on azinphos-methyl from 1966 through 1979. The 1981 report is the latest one available, which cites 71 incidents associated with human injury. There was one fatality which was a confirmed suicide. The PIMS report cited one bird kill and 29 incidents involving fish and other aquatic organisms. For the period 1978-1985, seven additional fish kills, citing azinphos-methyl, alone, were obtained at the Agency's Office of Water.

4. Summary of Regulatory Position

A. The Agency is requiring extensive field monitoring data to better define the extent of exposure and hazard to wildlife.

B. No new tolerances or new food uses will be considered until the Agency has received data sufficient to assess existing tolerances for azinphos-methyl.

C. The Agency is concerned about the potential for human poisonings (cholinesterase inhibition) from the use of azinphos-methyl. The Agency will continue to restrict all liquid formulations of azinphos-methyl with greater than 13.5% a.i. In addition, registrants must either classify all products for restricted use (due to acute toxicity) or submit dermal and inhalation data to support the appropriate toxicity category.

D. Revised Protective clothing statements are required to be included on the labels of azinphos-methyl end-use products.

E. The Agency has concluded that data are not adequate to determine the oncogenic potential of azinphos-methyl and is requiring numerous toxicology studies mentioned below.

F. The Agency is requiring that endangered species labeling be added to labels for certain azinphos-methyl uses.

G. A 24 hour re-entry interval, previously established under 40 CFR 170.3 (b)(2) will remain in effect.

H. The Agency is imposing an interim rotational crop restriction of 6 months for root crops and 30 days for all other registered crops until the required crop rotation data are submitted.

5. Summary of Major Data Gaps

-Additional crop residue studies on various commodities and plant and animal metabolism studies are required to support existing tolerances.
-The following studies are required to assess the toxicological characteristics of technical azinphos-methyl:
Acute inhalation, Delayed Neurotoxicity,
Oncogenicity/ Chronic testing in rat, Teratology, Reproduction, Mutagenicity, and General Metabolism.
-The following data are required to fully characterize azinphos-methyl's environmental fate: Re-entry data (foliar dissipation, soil dissipation, dermal exposure, inhalation exposure),

Special Testing-Glove Permeability, Photodegradation, Anaerobic Aquatic*, Forestry Dissipation*, Rotational Crops (Confined), Irrigated Crops Accumulated Study*, Accumulation in Non-target Organisms*

-Additional data are required to assess the impact on wildlife from the use of azinphos-methyl: acute avian oral toxicity, wild mammal toxicity, avian reproduction, field testing for mammals and birds, acute toxicity to freshwater invertebrates, acute toxicty to estuarine and marine organisms, fish early life stage, simulated or actual field testing for aquatic organisms and honey bee toxicity.

-Product chemistry and acute toxicity data are required.

*Data not needed if label clarifications are made.

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